

### REMARKS

Responsive to the Restriction Requirement mailed July 31, 2002, Applicants elect the invention of Group I (claims 1-3, 5-7, 13, 15-16 and new claims 24-27) drawn to a B cell epitope peptide of *Mycobacterium Tuberculosis* HSP 65 and a vaccine containing such an epitope peptide. This election is made without traverse.

Further, Applicants elect the species of SEQ ID NO:2 (peptide 6) of the claimed Group I invention. The claims readable thereon include amended claims 1-2, original claims 5-7, 13 and 15-16, and new claims 24 and 26.

In view of the present amendment, Applicants respectfully traverse the requirement for species election among SEQ ID NOs:1-3. SEQ ID NOs:1-3 are highly related peptide sequences. SEQ ID NO:1 contains amino acids 31-52 of the *Mycobacterium Tuberculosis* HSP 65 (SEQ ID NO:6). SEQ ID NOs:2 and 3 are two overlapping subsets of SEQ ID NO:1. SEQ ID NO:2 contains the N-terminal 16 amino acids of SEQ ID NO:1 (i.e., amino acids 31-46 of SEQ ID NO:6), and SEQ ID NO:3 contains the C-terminal 16 amino acids of SEQ ID NO:1 (i.e., amino acids 37-52 of SEQ ID NO:6). They overlap with each other by 10 amino acids (i.e., amino acids 37-46 of SEQ ID NO:6). As such, a single search (with SEQ ID NO:1) would reveal prior art for all three peptide sequences. Applicants therefore request that the requirement for species election be withdrawn.

Applicants have amended claim 1 to make it a generic claim that excludes the prior art yet covers all three peptide species, SEQ ID NOs:1-3. Original claim 1 has been rewritten as new claim 24, properly depending from amended claim 1. Claims 2-3 have been amended to promote clarity. Support for amended claims 1-3 and newly added claims 24-27 can be found, e.g., at page 4, lines 16-21, of the specification. No new matter has been introduced by the present amendment.

In addition, Applicants have corrected the formal drawings by separating Fig. 1 into Figs. 1A and 1B. Copies of these figures are attached with the changes marked in red. Accordingly, the description of Fig. 1 (page 4, line 2) and a reference to Fig. 1 (page 19, line 2) in the specification have been amended. For consistency, sequence P06806 described at page 4,

Applicant : Yaakov Naparstek, et al.  
Serial No. : 09/847,637  
Filed : May 2, 2001  
Page : 5

Attorney's Docket No.: 13125-002001 / 6433/US/99/CIP

line 3, should be referred to as "*Mycobacterium Tuberculosis* HSP 65" at page 4, line 2, so that change was made, as well.

Attached is a marked-up version of the changes being made by the current amendment.

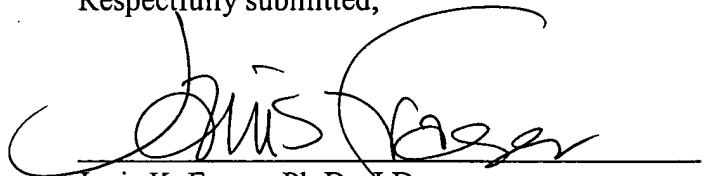
Applicants respectfully ask that claims 1-3, 5-7, 13, 15-16, and 24-27 be examined and allowed.

Enclosed is a \$36 check for the excess claims fee. Please apply any other charges to Deposit Account No. 06-1050, referencing attorney docket no. 13125-002001.

Respectfully submitted,

Date:

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**Version with markings to show changes made**

**In the specification:**

The paragraph beginning at page 4, line 2, has been replaced with the following rewritten paragraph:

[Fig. 1] Figs. 1A and 1B, *Mycobacterium Tuberculosis* HSP 65, rat HSP 60 and human HSP 60 (sequences P06806, P19227 and P10809, corresponding to SEQ ID NOs:6, 7 and 8 respectively), were compared with pileup program from GCG-Wisconsin Package v.9.0. The conserved regions are indicated (consensus). Bold, underlined residues represent the preferred peptides.

The paragraph beginning at page 19, line 2, has been replaced with the following rewritten paragraph:

The HSP 60 family is highly conserved: MT-HSP 65 and its mammalian homologues (rat or human) show 48% identity. In [Fig. 1] Figs. 1A and 1B, the three amino acid sequences of the MT-HSP 65, HSP 60 from rat and human are compared. The consensus sequence of these three proteins is shown too. The epitopes that were found to be relevant in this study are shown in Bold and Underlined.

**In the claims:**

Claims 1-3 have been amended as follows:

1. A B cell epitope peptide [comprising the amino acid sequence as denoted by SEQ ID NO:1], the sequence of which comprises SEQ ID NO:1 or a portion thereof that is selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:3.
2. [A] The B cell epitope peptide [as claimed in] of claim 1, [having the amino acid sequence as denoted by] the sequence of which consists of SEQ ID NO:2.

Applicant : Yaakov Naparstek, et al.  
Serial No. : 09/847,637  
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Page : 7

Attorney's Docket No.: 13125-002001 / 6433/US/99/CIP

3. [A] The B cell epitope peptide [as claimed in] of claim 1, [having the amino acid sequence as denoted by] the sequence of which consists of SEQ ID NO:3.



		1	6	25
HSP 65 - <u>M.T.</u>	-----	-----	MAKTI	AYDEEARRGL ERGLNALADA
HSP 60 - <u>RAT</u>	MLRLPTVLRQ	MRPVSRLAP	HLTRAYAKDV	KFGADARALM LQGVDLLADA
HSP 60 - <u>HUMAN</u>	MLRLPTVFRQ	MRPVSRLAP	HLTRAYAKDV	KFGADARALM LQGVDLLADA
Consensus	-----	-----	AK--	----AR--- --G---LADA

		26		75
HSP 65 - <u>M.T.</u>	VKVTLGPKGR	NVVLEKKWGA	PTITNDGVSI	AKEIELEDPY EKIGAELVKE
HSP 60 - <u>RAT</u>	VAVTMGPKGR	TVIIEQSWGS	PKVTKDGVTV	AKSIDLKDKY KNIGAKLVQD
HSP 60 - <u>HUMAN</u>	VAVTMGPKGR	TVIIEQSWGS	PKVTKDGVTV	AKSIDLKDKY KNIGAKLVQD
Consensus	V-VT-GPKGR	-V--E--WG-	P--T-DGV--	AK-I-L-D-Y --IGA-LV--

6-7 (31-52 AA)

		76		125
HSP 65 - <u>M.T.</u>	VAKTDDVAG	DGTTTATVLA	QALVREGLRN	VAAGANPLGL KRGIEKAVEK
HSP 60 - <u>RAT</u>	VANNTNEEAG	DGTTTATVLA	RSIAKEGFEX	ISKGANPVEI RRGVMLAVDA
HSP 60 - <u>HUMAN</u>	VANNTNEEAG	DGTTTATVLA	RSIAKEGFEX	ISKGANPVEI RRGVMLAVDA
Consensus	VA--T---AG	DGTTTATVLA	-----EG---	---GANP--- -RG---AV--

21 (121-136 AA)

		126		174
HSP 65 - <u>M.T.</u>	VTETLLKGAK	EZETKEQIAA	TAAISA.GDQ	SIGDLIAEAM DKVGNVGVIT
HSP 60 - <u>RAT</u>	VIAELKKQSK	PVTTPEEIAQ	VATISANGDK	DIGNIISDAM KKVGRKGVIT
HSP 60 - <u>HUMAN</u>	VIAELKKQSK	PVTTPEEIAQ	VATISANGDK	EIGNIISDAM KKVGRKGVIT
Consensus	V---L-K--K	-V-T-E-IA-	-A-ISA-GD-	-IG--I--AM -KVG--GVIT

		175		224
HSP 65 - <u>M.T.</u>	VEESNTFGLQ	LELTEGMKFD	RGYISGYFVT	DPERQEAVLE DFIYLLVSSK
HSP 60 - <u>RAT</u>	VKDGTKLNDE	LEIIEGMKFD	RGYISPYFIN	TSKGQKCEFO DAYVLLSEKK
HSP 60 - <u>HUMAN</u>	VKDGTKLNDE	LEIIEGMKFD	RGYISPYFIN	TSKGQKCEFO DAYVLLSEKK
Consensus	V----T----	LE--EGM-FD	-GYIS-YF--	----Q----- D-Y-LL---K

31 (181-196 AA)

36 (211-226 AA)

		225		274
HSP 65 - <u>M.T.</u>	VSTVKDLLPL	LEKVIAGAKP	LLIIAEDVEG	EALSTLVVNK IRGTFKSVAV
HSP 60 - <u>RAT</u>	ISSVQSIVPA	LEIANAHKRP	LVIIAEDVDG	EALSTLVNLR LKVGLOVVAV
HSP 60 - <u>HUMAN</u>	ISSIQSIVPA	LEIANAHKRP	LVIIAEDVDG	EALSTLVNLR LKVGLOVVAV
Consensus	-S-----P-	LE-----KP	L-IIAEDV-G	EALSTLV-N- -----VAV

40 (236-251 AA)

45 (265-280 AA)

Fig. 1A



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275. 323  
HSP 65 - M.T. KAPGFGDRRK AMLQDMAILT GGQVISEE.V GLTLENADLS LLGKARKVVV  
HSP 60 - RAT KAPGFGDNRK NQLKDMAIAT GGAVFGEEGL NLNLEDVQAH DLGKVGEVIV  
HSP 60 - HUMAN KAPGFGDNRK NQLKDMAIAT GGAVFGEEGL TLNLEDVQPH DLGKVGEVIV  
Consensus KAPGFGD-RK --L-DMAI-T GG-V--EE-- -L-LE----- -LGK---V-V

324 373  
HSP 65 - M.T. TKDETTIVEG AGDTDAIAGR VAQIRQEIEN SDSDYDREKL QERLAKLAGG  
HSP 60 - RAT TKDDAMLLKG KGDKAHIEKR IQEITEQLDI TTSEYERERL NERLAKLSDG  
HSP 60 - HUMAN TKDDAMLLKG KGDKAQIEKR IQEIIIEQLDV TTSEYERERL NERLAKLSDG  
Consensus TKD-----G -GD---I--R ---I----- --S-Y--EKL -ERLAKL--G

59 (349-364 AA)

374 423  
HSP 65 - M.T. VAVIKAGAAT EVELKERKHR IEDAVRNAKA AVEEGIVAGG GVTL LQAAPT  
HSP 60 - RAT VAVLKVGGS DVEVNEKKDR VTDALNATRA AVEEGIVLGG GCALLRCIPA  
HSP 60 - HUMAN VAVLKVGGS DVEVNEKKDR VTDALNATRA AVEEGIVLGG GCALLRCIPA  
Consensus VAV-K-G--- -VE--E-K-R --DA-----A AVEEGIV-GG G--LL---P-

63 (373-388 AA)

424 472  
HSP 65 - M.T. LDELK.LEGD EATGANIVKV ALEAPLKQIA FNSGLEPGVV AEKVRNLPAG  
HSP 60 - RAT LDCLKPANED QKIGIEIIR ALKIPAMTIA KNAGVEGSLI VEKILQSSSE  
HSP 60 - HUMAN LDCLKPANED QKIGIEIIR TLKIPAMTIA KNAGVEGSLI VEKIMQSSSE  
Consensus LD-L-----D ---G--I-K- -L--P---IA -N-G-E---- -EK-----

473 522  
HSP 65 - M.T. HGLNAQTGVY EDLLAAGVAD PVKVTRSALQ NAASIAGLFL TTEAVVADKP  
HSP 60 - RAT VGYDAMLGDF VNMVEKGIID PTKVVRTALL DAAGVAPLLT TAEAVVTEIP  
HSP 60 - HUMAN VGYDAMAGDF VNMVEKGIID PTKVVRTALL DAAGVASLLT TAEVVVTEIP  
Consensus -G--A-G-- -----G--D P-KV-R-AL- -AA--A-L-- T-E-VV---P

84 (499-514 AA)

523 540  
HSP 65 - M.T. EKEKASVPGG GDMGGMDF-- -----  
HSP 60 - RAT KEEKD..PGM GAMGGMGGGM GGGMF  
HSP 60 - HUMAN KEEKD..PGM GAMGGMGGGM GGGMF  
Consensus --EK---PG- G-MGGM-----

Fig. 1B